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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,922	11/03/2003	Johanna Bergmann	830006-2000	5900

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EXAMINER	
EMCH, GREGORY S	
ART UNIT	PAPER NUMBER
1649	
MAIL DATE	DELIVERY MODE
05/19/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/700,922	BERGMANN ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8 and 9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/26/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on 26 February 2008 has been entered.

Response to Amendment

Claims 8 and 9 have been amended as requested in the amendment filed on 26 February 2008. Following the amendment claims 8 and 9 are pending in the instant application.

Claims 8 and 9 are under examination in the instant office action.

Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicants' response and withdrawn.

Information Disclosure Statement

A signed and initialed copy of the IDS paper filed 26 February 2008 is enclosed in this action.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8 and 9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 8-9 are directed to a method of inducing an immune response against SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 5 comprising administering an antibody against SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 5, respectively.

The Examiner is unable to find any support in the disclosure as-filed for the instant limitations of "a method of inducing an immune response against SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 5 comprising administering an antibody against SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 5, respectively." Applicants are required to cancel the new matter in the response to this Office action. Alternatively, Applicants are invited to identify sufficient written support in the original specification for the "limitations" indicated above. Applicants' remarks, in the Response filed on 26 February 2008 do not provide sufficient direction for the written description for the above-mentioned limitations of claims 8 and 9. Here, Applicants assert, "Support is found, for example, in

paragraphs 83 and 125 of the specification as published." It is noted that the specification as published is not the same as the specification as filed. Applicants are advised that when pointing out support, Applicants should refer to the original specification and not the published specification. Regardless, paragraphs 83 and 125 of the published specification do not provide the requisite written description for the instant claimed method of inducing an immune response against SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 5 comprising administering an antibody against SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 5. Thus, the claims encompass new matter.

Claims 8 and 9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

The claims are drawn to a method of inducing an immune response against SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 5 comprising administering an antibody against SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 5, respectively.

The immune response is defined as the ability of any given cell in the body to distinguish self from non-self. (Immune response. (n.d.). *The American Heritage® Dictionary of the English Language, Fourth Edition*. Retrieved May 15, 2008, from Answers.com Web site: http://www.answers.com/topic/immune-response). Induction of an immune response can be induced by stimulating the immune system to respond to a protein that is administered, wherein endogenous antibodies to the protein are thereby produced. This is recognized by the art as "active immunization." The instant method, on the other hand, is directed to administering exogenous antibodies, recognized by the art as "passive immunization" (Immunization. (n.d.). Wikipedia. Retrieved May 15, 2008, from Answers.com Web site: http://www.answers.com/topic/immunization). Here, the exogenous antibodies may recognize an antigen present in a patient's blood and may thus bind to the antigen to sequester and inactivate it. Administration of antibodies does not stimulate an immune response; rather, it could be thought of as substituting for an immune response (hence, the term “passive” immunization vs. "active“ immunization wherein an immune response can be induced). Applicants' submitted prior art reference, i.e. the Kienzl et al. reference (cited on IDS dated 26 February 2008), supports the Examiner’s position. Applicants cite the second paragraph of the abstract in an assertion for enablement of the instant claims. However, this portion of the reference teaches, "Moreover, the expression of ALZAS is mirrored by a specific

autoimmune response. This autoimmune reaction detected in AD patients was found to be directed against the ct-12 end of the ALZAS-peptide and not against the Aβ-sequence. ELISA-studies from testing plasma revealed highest titers to be found in patients with obviously presymptomatic AD or mild cognitive impairment (MCI) and moderately increased titers in confirmed AD. Low or not detectable anti-ct12 titers characterized healthy age matched subjects or young controls. The antigen, ALZAS protein, could be detected in serum in later clinical stages of AD patients. It is suggested that ALZAS represents an indicator in a dynamic equilibrium between both peripheral and brain degenerative changes thus providing a simple diagnostic blood test." (Emphasis added). This excerpt describes how an immune response is directed against a protein and does not describe how an immune response would be directed against antibodies to the protein, as currently claimed. Other relevant prior art does not provide compensatory teachings, as the art is silent with respect to inducing an immune response with administration of antibodies, thus evidencing unpredictability in the art. Similarly, the specification does not provide compensatory teachings, as it is also silent with respect to inducing an immune response with administration of antibodies, either in the working examples or otherwise.

In the reply filed on 26 February 2008, Applicants again assert that undue experimentation does not necessarily follow from a lack of examples in the specification and that an applicant need not describe all actual embodiments of a claimed invention. Applicants also again assert that they "used a procedure which they had successfully used to find alternative genes, which are putative causative factors of other 'genetic

diseases', to search for such genes which might segregate with Alzheimer's disease, within the locus encoding the entire APP gene on chromosome 21 and the regions that flank the gene…Therefore, based upon the Applicants' disclosure, one of skill in the art would believe that ALZAS proteins are not mere markers but rather causative agents of Alzheimer's disease or associated diseases." Applicants allege that the Kienzl et al. reference (cited on IDS dated 26 February 2008) teaches that "an ALZAS protein elicits an autoimmune response in patients (see, e.g., second paragraph of the abstract)." Therefore, Applicants assert that the specification is enabling for the present claims that recite methods for inducing an immune response. Applicants assert that based on the instant disclosure, the skilled artisan would recognize that "ALZAS proteins are causative agents of Alzheimer's disease or associated diseases, that ALZAS proteins are modulated by the immune system in patients with Alzheimer's disease and that administration of antibodies against ALZAS proteins would result in eliciting an immune response against ALZAS proteins." Applicants assert that there is no factual evidence corresponding to the Wands factors, that the 35 U.S.C. 112 rejection is improper and must be withdrawn.

Applicants' arguments have been fully considered and are not found persuasive. Again, the Examiner agrees that undue experimentation does not necessarily follow from a lack of working examples in the specification and that an applicant need not describe all actual embodiments of a claimed invention. However, in the instant case, Applicants have not described any of the actual embodiments such that the skilled artisan can practice the claimed invention without undue experimentation. MPEP

2164.06 (b) states that in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), the court concluded that undue experimentation would not be required to practice the invention because "the specification provided considerable direction and guidance on how to practice the claimed invention and presented working examples, that all of the methods needed to practice the invention were well known, and that there was a high level of skill in the art at the time the application was filed. Furthermore, the applicant carried out the entire procedure for making a monoclonal antibody against HBsAg three times and each time was successful in producing at least one antibody which fell within the scope of the claims." Contrary to the disclosure in *In re Wands*, the instant specification does not present sufficient guidance for the claimed invention because the specification has presented no working example; the methods are complex and unpredictable and are not at all established in the art. Although the level of skill in the art is high, the art indicates that the instant invention would not work, i.e. it indicates that particular peptides, and not antibodies to the peptides, induce an immune response. Thus, the claims are deemed to lack enablement, since the Wands factors are not met, and not only because there are no working examples.

Applicants' assertion that based upon Applicants' disclosure and based on the Kienzl et al. reference, the skilled artisan "would believe that ALZAS proteins are not mere markers but rather causative agents of Alzheimer's disease or associated diseases" is not persuasive. As stated previously, the expression data presented in the specification is correlative only. Just because a biological molecule correlates with the presence of a disease does not mean it is a therapeutic target. The molecule may

accumulate as a *result* of the disease and thus may not play a *causative* role or a role in disease *progression*. The Kienzl et al. reference supports the Examiner's position since it explicitly states, "It is suggested that ALZAS represents an indicator in a dynamic equilibrium between both peripheral and brain degenerative changes thus providing a simple diagnostic blood test." (Emphasis added.) Therefore, the skilled artisan would recognize the potential diagnostic utility of the ALZAS protein and would not automatically believe that ALZAS proteins are causative agents of Alzheimer's disease or associated diseases.

Since the claims encompass inducing an immune response via administration of antibodies and given the art-recognized unpredictability of practicing such an invention, the lack of data or evidence supporting the claimed method either in the specification or in the prior art, the complex and unpredictable nature of the invention, it would require undue experimentation for one of skill in the art to practice the claimed invention. Therefore, the instant rejection is properly maintained.

Conclusion

No claims are allowed.

Applicants' request for an interview submitted with the previous reply is acknowledged. As this case is due for action, the Examiner has prepared the instant communication in the interest of being timely. Applicants are invited to contact the Examiner by phone to request an interview once they have reviewed the instant action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Patent Examiner
Art Unit 1649
15 May 2008

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